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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/777,566	02/05/2001	Jay M. Short	DIVER1370-6	4776

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/777,566	SHORT ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 16-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,16-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/24/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Abstract*.

DETAILED ACTION

Status of the Application

Claims 1-13 and 16-46 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/2004 has been entered.

Applicant's amendment of claims 1-4, 10-12, 16, 21, 24-27, 32-33, cancellation of claims 14-15, addition of claims 35-46, and a declaration under 37 CFR 1.132 by Dr. Jay Short, in a communication filed on 5/19/2004 are acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

1. The specification is objected to for the following reasons. The disclosure (paragraph 109 of U.S. Publication No. 2001/0055788) indicates that the polynucleotide encoding SEQ ID NO: 2 contains an open reading frame encoding a protein of 432 amino acids. SEQ ID NO: 2 according to the sequence listing contains 440 amino acids. SEQ ID NO: 1 was found to encode all 440 amino acids of SEQ ID NO: 2. While it appears that the polypeptide of SEQ ID NO: 2 comprises a His tag at the C-terminus, this tag is 6 amino acids long. Thus, even if one does not consider the His tag, the remaining polypeptide would have 434 amino acids and not 432 amino acids as asserted. Clarification is required.

Claim Objections

2. Claim 16 is objected to due to the recitation of "wherein the host cell is capable of expressing the exogenous..., and the exogenous nucleic...., and the polypeptide having phytase...". For clarity, it is suggested that the first "and" be deleted, i.e. "wherein the host cell is capable of expressing the exogenous..., the exogenous nucleic...., and the polypeptide having phytase...". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 21-23, 34 remain rejected and newly added claims 35-44, 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 21 (claim 22 dependent thereon) is indefinite in the recitation of "wherein the nucleic acid further comprises a vector sequence" for the reasons of record. Applicant's arguments regarding the term "comprises" as open ended language have been considered but are not deemed persuasive to overcome the rejection for the following reasons. As known in the art, vectors are large nucleic acids which may comprise protein encoding nucleic acids. Since the nucleic acid being referred to in the claim encodes a protein, it is unclear as to how this protein encoding nucleic acid can comprise a larger nucleic acid (vector) or the sequence of a larger nucleic acid. For examination purposes, it will be assumed that the term reads "wherein the nucleic acid is comprised in a vector". Correction is required.

6. Claims 22-23 are indefinite in the recitation of "wherein the vector comprises a cloning vector, an expression vector....., chromosomal DNA sequences , nonchromosomal DNA sequences, synthetic DNA sequences, a vaccinia vector...or a combination thereof" for the reasons of record. Applicant's arguments

regarding the term "comprises" as open ended language have been considered but are not deemed persuasive to overcome the rejection of these claims for the following reasons. The term "comprises" as recited implies that the vector contains the items listed. While the term "vector comprises" is definite as it relates to DNA sequences, the term is indefinite as it relates to the different vectors recited since it is unclear as to how a vector can contain another vector. Similarly, the term "combination thereof" is indefinite since it is unclear as to how a vector can contain combinations of other vectors. For examination purposes, it will be assumed that the claims recite "wherein the vector is a cloning vector, an expression vector, a bacterial vector, a plasmid, a viral particle, a phage, a vaccinia vector, an adenovirus vector, a fowl pox virus, or a pseudorabies vector, and wherein said vector comprises chromosomal DNA sequences, nonchromosomal DNA sequences, non-naturally occurring DNA sequences or chemically synthesized DNA sequences". Correction is required.

7. Claim 34 is indefinite in the recitation of "wherein the phytase activity comprises hydrolyzing inorganic phosphate from phytate" as it does not further limit claim 16. As known in the art, phytases hydrolyze inorganic phosphate from phytate, therefore this activity is inherent to phytases. Applicants argue that since enzymes catalyze a reaction in both directions, claim 34 is further limiting claim 16. These arguments are not deemed persuasive. While it is agreed that in theory an enzyme can catalyze a reaction in both directions, it is noted that the art recognizes the hydrolysis of phosphate from phytate to inorganic phosphate as the enzymatic activity associated with phytases, and not the reverse reaction. See, for example, the Abstract by Casey et al. (J. Biotechnology 110(3):313-322, 2004). For examination purposes, claim 34 will be considered a duplicate of claim 16. Correction is required.

8. Claims 35-44 and 46 are indefinite in the recitation of "comprising a sequence that is the complement of a sequence of ..." because it is unclear which complement is being referred to. Fragments of any size which are complementary to the nucleotide sequences recited can be considered as "complements". Applicants have not define the term "complement", as it relates to size, in the

specification either. If Applicant's intended complement is the entire complement, it is suggested that the term "complement" be replaced with "complete complement". For examination purposes, the suggested language will be used. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-13, 16-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection necessitated by Applicant's amendment.

Claims 1-3, 16-46 are directed to a recombinant expression system, a cell, or a vector comprising a polynucleotide encoding amino acids 1-432 of SEQ ID NO: 2, as well as a method for making a phytase with a cell comprising a polynucleotide encoding amino acids 1-432 of SEQ ID NO: 2. While SEQ ID NO: 2 has been disclosed, the Examiner is unable to locate adequate support in the specification for an expression system, a cell, or a vector comprising a polynucleotide encoding amino acids 1-432 of SEQ ID NO: 2. Also, no support could be found for a method for making a phytase with a cell comprising a polynucleotide encoding amino acids 1-432 of SEQ ID NO: 2. Thus, there is no indication that the claimed invention was within the scope of the invention as conceived by Applicants at the time the application was filed. Accordingly, Applicants are required to cancel the new matter in response to this Office Action.

11. Claims 2, 10-13, 16-17, 20-34 remain rejected and new claims 35-44, 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been discussed at length in previous Office Actions and is now applied to newly added claims 35-44 and 46 for the reasons of record and those set forth below.

12. Applicants argue that after the instant amendment, the claims will be clearly directed to vectors, cells or expression systems comprising a genus of nucleic acids encoding polypeptides having phytase activity. Furthermore, Applicants submit that only structurally and functionally related nucleic acids are encompassed by the scope of the claims and that the nucleic acids of the invention are described by their structure, a physico-chemical property, and function. Thus, it is Applicant's opinion that the genus of nucleic acids recited in the claims is adequately described. Applicants further refer to Dr. Short's declaration (inventor) and state that according to Dr. Short, procedures to identify polypeptides having phytase activity and making polynucleotides which encode the many variants of the polypeptide of SEQ ID NO: 2 having any number of conservative substitutions, as recited in the claims, were conventional and routine in the art at the time of the invention. Applicants refer to Example 14 of the USPTO Written Description Guidelines as shown in Exhibit A and assert that the instant claims recite polynucleotides which are defined by structure and function. Applicants further submit that the claims fully comply with the written description requirements as set forth in *University of California v. Eli Lillv & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) and conclude that those of skill in the art would recognize Applicant's possession of the claimed invention, citing *Vas-cath Inc. V. Mahukar,* 19 USPQ2d 1 111, (Fed Cir. 1991). Applicants further submit that the disclosed function for the polypeptides encoded by the recited nucleic acids, i.e. phytase, is sufficiently correlated to a particular known structure, i.e. the polypeptide of SEQ

ID NO: 2, and a physical property (i.e. specific conservative amino acid substitutions based on interchange of aliphatic residues, hydroxyl-comprising residues, acidic residues, amide residues, basic residues, or aromatic residues).

13. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 2, 10-13, 16-17, 20-34 or avoid the rejection of claims 35-44, 46. The Examiner acknowledges inventor Jay Short's declaration and agrees that the claims now recite nucleic acids which encode polypeptides having phytase activity. However, the Examiner disagrees with Applicant's contention that the claimed invention is adequately described. Claims 2, 10-13, 16-17, 20-44 and 46 are directed to (1) an expression system, vector or host cell comprising nucleic acids encoding phytases wherein said phytases are variants of the polypeptide of SEQ ID NO: 2 which result from any number of conservative substitutions, or (2) a method of making a phytase using the host cells of (1). While the specification discloses one species of the claimed polynucleotides, i.e. a polynucleotide which encodes the polypeptide of SEQ ID NO: 2, the specification is completely silent in regard to which amino acid substitutions in the polypeptide of SEQ ID NO: 2 would result in a polypeptide having the same phytase activity associated with the polypeptide of SEQ ID NO: 2, nor does it provide any clue as to the correlation between the structure of SEQ ID NO: 2 and phytase function.

The written description guidelines indicate that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus, A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of

species to reflect the variation within the genus. As indicated in the previous Office Action, the art teaches that even highly structurally similar homologs do not necessarily share the same function. In the instant case, the genus of nucleic acids recited can encode polypeptides sharing anywhere from 0%-99.8% sequence identity. As known in the art, identity is calculated taking only into consideration exact matches. Thus, if all the amino acids of SEQ ID NO: 2 are replaced with conservative substitutions, the % sequence identity is 0%. If on the other hand, only one substitutions is made in the polypeptide of SEQ ID NO: 2 (440 amino acids), then the % identity is 99.8% (439x100/440). The structural variation within the nucleic acids encompassed by the claims is so large that one of skill in the art cannot reasonably conclude that a single species is sufficient to adequately describe the entire genus, particularly in view of the fact that the specification is completely silent regarding any correlation between phytase function and structure. It is reiterated herein that the structural features common to the members of the genus, i.e. encoding a polypeptide which results from any number of conservative substitutions in the polypeptide of SEQ ID NO: 2, does not constitute a substantial portion of the genus as the remainder of any nucleic acid comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

14. Claims 2, 10-13, 16-17, 20-34 remain rejected and new claims 35-44, 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding the polypeptide of SEQ ID NO: 2, a vector and a host cell comprising said nucleic acid, as well as a method of recombinantly producing the polypeptide of SEQ ID NO: 2 in a cell, does not reasonably provide enablement for (1) an expression system, vector or host cell comprising a nucleic acid which encodes a phytase, wherein said phytase has the amino acid sequence of SEQ ID NO: 2 with any number

of conservative substitutions, or (2) a method to produce a phytase with the host cell of (1). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been discussed at length in previous Office Actions and is now applied to newly added claims 35-44 and 46 for the reasons of record and those set forth below.

15. Applicants argue that the instant amendment addresses the issue of "any function" since the genus of nucleic acids recited must encode phytases. Applicants refer to a declaration by inventor Jay Short, who declares that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art was very high. Dr Short's declaration further states that one of skill in the art at the time of the invention could use the teachings of the specification and other protocols known in the art to make variants of the polypeptide of SEQ ID NO: 2 which result from any number of conservative amino acid substitutions and screen them for phytase activity. Furthermore, according to Dr. Short's declaration, while the number of samples needed to be screened may have been high, the screening procedures were routine and successful results predictable. According to Dr. Short's declaration, knowledge of the specific structural elements which correlate with phytase activity would not have been required to create variants and test them for activity. Applicants further argue that enablement is not precluded by the necessity to screen large number of compositions as long as that screening is routine. Applicants refer to *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* as support for the argument that the claimed invention is enabled even if there is a need to screen numbers of negatives to find a sample with the desired activity.

16. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 2, 10-13, 16-17, 20-34 or avoid the rejection of claims 35-44, 46. The Examiner acknowledges inventor Jay Short's declaration and agrees that the claims now recite nucleic acids which encode polypeptides having phytase function. However, the Examiner disagrees with Applicant's

contention that the claimed invention is adequately described. The scope of claims 2, 10-13, 16-17, 20-44 and 46 is not commensurate with the enablement provided in view of the infinite number of nucleic acids encoding polypeptides having phytase activity encompassed by the claims for which no correlation between function and structure has been provided. As indicated above, the specification is completely silent in regard to which amino acid substitutions in the polypeptide of SEQ ID NO: 2 would result in a polypeptide having the same phytase activity associated with the polypeptide of SEQ ID NO: 2. There is no teaching as to which are the structural elements in the polypeptide of SEQ ID NO: 2 which can be conservatively substituted and still retain phytase activity. The art, as evidenced by Broun et al., Witkowski et al. and Seffernick et al., clearly teaches the unpredictability of assigning function based on structural homology and how small structural changes can lead to major changes in function. Therefore, in the absence of any information as to how structure correlates with function, one of skill in the art would have to go through the burden of undue experimentation to isolate/make the nucleic acids as encompassed by the claims, to practice the full scope of the claimed invention.

The Examiner acknowledges the ruling in *Hybritech, Inc. v. Monoclonal Antibodies, Inc* as well as the declaration by inventor Jay Short, and agrees that enablement is not precluded by the need of screening a number of compositions as long as the screening is routine. Furthermore, the Examiner agrees that creation of nucleic acids having the structural limitations recited in the claims and testing for phytase activity is routine in the art. However, the Examiner disagrees with Applicant's contention that testing the extremely large number of nucleic acids encompassed by the claims is not undue experimentation when there is no guidance or knowledge as to which are the structural elements in the polypeptide of SEQ ID NO: 2 that correlate with phytase activity. The claims encompass an extremely large number of possible substitution combinations (2^N-1, where N=440) since any position in the polypeptide of SEQ ID NO: 2 can be substituted. It is not routine in the art to randomly create an infinite number of variants and test them for activity. Instead, as indicated above, one of skill in the art would

have some knowledge or guidance as to how structure correlates with function such that a reasonable number of variants with the potentiality of having the desired function can be created and tested. Thus, in view of the information provided, the lack of relevant examples, the lack of knowledge about the critical structural elements required for phytase activity, and the unpredictability of the art in regard to accurate annotation of function based on structural homology, one of skill in the art cannot reasonably conclude that the specification is enabling for the full scope of the claimed invention.

Double Patenting

17. Claims 1-13, 16-27, 29-32, 34 remain provisionally rejected and new claims 35-46 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15, 17-26, 91-94 of copending Application No. 10/430356.

18. Applicants will hold this issue in abeyance until the instant claims are found allowable.

19. This rejection has been discussed at length in the previous Office Action and is now applied to new claims 35-46 for the reasons of record. Since no terminal disclaimer has been filed and no arguments have been presented pointing out disagreements with the Examiner's contentions, the obviousness-type double patenting rejection is maintained.

20. Applicant is advised that should claims 37 and 43 be found allowable, claims 39 and 44 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

21. No claim is in condition for allowance.

22. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
June 15, 2004